

The prognostic value of normal myocardial perfusion spect with positive coronary angiography

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Abstract

BACKGROUND: Normal exercise SPECT studies are associated with a low event rate. The association of the negative SPECT and positive coronary angiography with the results for the long time follow up was determined.

MATERIAL AND METHODS: 45 patients were included into the study. All patients had normal SPECT study and positive angiography in the ≤ 6 months after SPECT. 20 of them were women. Six patients had diabetes mellitus, 8 was smokers. Two patients had had left main coronary artery and 12 had multivessel disease. Baseline clinical risk factors were recorded for each patients and compared to outcomes.

RESULTS: There were no deaths in the study group in the follow up period. One myocardial infarct occurred in patient with multivessel disease and five more angioplasties with stents were performed in the long term follow up due to progression of coronary stenosis.

CONCLUSIONS: We observed that the normal SPECT with positive ECG pattern is infrequent and has a very good prognostic value. However, the long-term survival among a patient cohort with a normal exercise SPECT study is influenced by the number of concomitant CAD risk factors. We conclude that there

is an importance of modifying CAD risk factors among patients with a normal SPECT.

Key words: exercise SPECT, cardiac risk factors, coronary artery disease

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Introduction

A number of authors have demonstrated that patients with chest pain and negative myocardial perfusion scintigraphy results have a very good prognosis with $< 1\%$ per year mortality and incidence of infarction [1–10]. Even when the results of angiography are known, radionuclide tests may provide incremental information for patients risk stratification. Despite increasing emphasis on the potential long-term and even lifetime risk associated with CAD (coronary artery diseases) risk factors in the general population, studies regarding the long-term influence of CAD risk factors among patients undergoing stress SPECT myocardial perfusion imaging are remarkably limited.

To determine the prevalence of negative myocardial perfusion single-photon emission computerized tomography (SPECT) results associated with positive coronary angiography for the long time follow up we reviewed all SPECT studies performed in our center over a period of 5 years.

Material and methods

We conducted a retrospective evaluation of 4324 myocardial perfusion SPECT studies performed in our center between 2000 and 2005. All patients underwent symptom limited treadmill exercise testing using the Bruce protocol and at peak heart rate (85% maximal predicted heart rate), 25–30 mCi of ^{99m}Tc MIBI was injected. All SPECT studies were acquired on Siemens Ecam gamma camera.

All stress and rest SPECT data were analyzed by two readers separately for both perfusion and wall motion abnormalities if

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Table 1. Baseline patient characteristics of all patients and according to those who had revascularization at follow up

	All patients (n = 45)	Without revascu- larization (n = 38)	After revascu- larization PTCA (n = 5) CABG (n = 2)
Age (years)	64 ± 7	63 ± 10	69 ± 5
Male	25	20	PTCA — 3 pts CABG — 2 pts
Hypertension	12 pts	10 pts	CABG — 2 pts
Diabetes mellitus	6 pts	—	CABG — 6 pts
Dyslipidemia	29 pts	22 pts	PTCA + CABG — 7 pts
Smoking	8 pts	3 pts	PTCA — 4 pts CABG — 1 pts
Family history	40 pts	33 pts	PTCA — 5 CABG — 2

the gated SPECT was performed. A semi-quantitative visual interpretation was performed using segmentation of short-axis slices into apical, mid, and basal slices and vertical long-axis myocardial tomograms. Studies were classified as normal, equivocal, or abnormal due to ischemia and or infarction. All images were subsequently reviewed for possible presence of heart failure indicated by the left ventricular dilatation in stress images. Only patients determined to have normal perfusion and normal gated SPECT images were included in this study. Finally, we selected 45 patients with normal baseline ECG, positive exercise ECG and normal SPECT, referred for coronary angiography by the clinical cardiologists.

Results

Baseline characteristics of study patients are presented in Table 1. Among 45 our patients, 20 were women, 40 (88.8%) had at least one risk factor (12 — hypertension; 29 — dyslipidemia,

6 — type 2 diabetes, 8 — smoking and 40 — family history of CAD). Pulmonary uptake or transient ischemic dilation of the left ventricle were not found in any patient. Results of the exercise test for these patients appear in Table 2. Before exercise testing, 10 women and 1 man were not taking anti-angina medication; 11 patients (7 women) were taking beta-blockers; 11 patients (10 women), calcium antagonists; 11 patients (10 women), nitrates, and 16 patients (10 women), antiplatelet drugs. All patients had positive exercise test and normal ^{99m}Tc MIBI SPECT perfusion images.

All 45 patients underwent coronary angiography using Sel-dinger's technique at ≤ 6 months after the SPECT study, assuming no previous complications. Coronary angiography findings for these patients appear in Table 3. One of the 20 women had 40% stenosis of the left main coronary artery, 6 had 1 and 14 had 2-vessel disease. One of the 25 men had 50% stenosis of the left main coronary artery, 8 had multivessel disease and 16 had one vessel disease.

Follow-up

There were no deaths in the study group in the follow up period. One myocardial infarct occurred in patient with multivessel disease and five more angioplasties with stents were performed in the long term follow up due to progression of coronary stenosis (Table 4).

Discussion

We observed the low prevalence of patients with normal SPECT and positive ECG, in our study 1%, similar to the 2–3.5% range described in other studies [11–13]. Our study demonstrates that the follow up of patients associated with a normal exercise SPECT study is extended over a long-term among patients with normal exercise SPECT studies and 0–1 risk factors for CAD. Previous studies found that the low risk is independent of imaging type (SPECT versus PET), the type of stress performed (exercise versus pharmacological) patients clinical characteristics, the radio-tracer used, patients prior history of CAD, the results of stress testing and many other factors [14–17]. Ellehendi et al. [18] followed a group of 218 patients with and without known CAD who were

Table 2. Medications and exercise test results

	All patients (n = 45)	Without revascularization (n = 38)	After revascularization PTCA (n = 5) CABG (n = 2)	P value
Beta blockers	10	4	6	< 0.001
Calcium channel blockers	11	10	1	
Antiplatelet drugs	16	9	7	
ACE inhibitors	10	8	2	
Statins	25	18	7	< 0.001
Nitrates	17	15	2	
METs	8.0 ± 2	8.1 ± 2	7.1 ± 3	
Exercise duration	8.1 ± 3	8.3 ± 2	7.1 ± 2	
Peak HR	147 ± 16	149 ± 19	147 ± 12	
ST segment response ischemic (≥ 1 mm)	45	38	7	

Table 3. Results of coronary nagiography

	All patients (n =45)	Women	Men	Mean Number of CAD risk factors
One vessel disease	21	7	14	1.2 ± 1
Two vessel disease	10	10		1.3 ± 1
Multivessel vessel disease	12	7	5	1.2 ± 1
Left main stenosis	2	1 (40% stenosis)	1 (50% stenosis)	1.1 ± 1

Table 4. Characteristics of patients after PTCA and MI in the follow up

	Age(years)	Hypertension	Diabetes	Dyslipidemia	Smoking	Family history
PTCA (n = 5)	61 ± 2.1	4	–	10	3	5
MI (n = 1)	64	+	–	+	+	+

undergoing exercise SPECT for 7.4 ± 1.8 years and found none of the established CAD risk factors to be predictive of cardiac events. Among patients undergoing stress echocardiography, McCully et al. [19] examined 1,325 patients with no known heart disease and a normal exercise echocardiogram during a mean follow-up of 2 years for a composite endpoint of all-cause mortality and cardiac events. The authors found that none of the traditional CAD risk factors were associated with a worse outcome. However in the prior literature assessing the normal SPECT study and positive coronary angiography, those with 0–1 CAD risk factors had an excellent long-term prognosis, those with multiple risk factors had a worse prognosis and must be considered at being at intermediate risk [20–26]. When taken individually, only diabetes, smoking, and hypertension were associated with an increase in mortality, but family history and a history of hyperlipidemia were not. Hachamovitch et al. [27, 28] found that among 6,046 patients without known CAD who underwent either exercise or pharmacologic stress SPECT (followed for 1.8 ± 0.5 years), only diabetes was a predictor of cardiac death and non-fatal myocardial infarction during follow-up. Among patients undergoing dobutamine stress echocardiography, Chaowalit et al. [30] followed 3,041 patients with and without a history of CAD for a mean follow-up of 6.3 years and also found only diabetes as a predictor of all-cause mortality; while Sozzi et al. [31] followed 417 patients over a mean follow-up of 5 years and found none of the established CAD risk factor to be a predictive of mortality. Thus, our data confirmed that the normal exercise SPECT study of a mean follow-up of 4.7 years among a patients with the variability of risk factors and positive coronary angiography had an excellent prognosis and but was depend of the risk factors, such as diabetes and smoking.

One possible cause of -negative myocardial perfusion SPECT studies in patients with positive exercise test may be the presence of diffuse coronary heart disease with homogeneous ischemia of the entire left ventricle, perfusion images of which fail to identify any single region with comparatively more reduced uptake. We found that most patients with coronary heart disease detected by coronary angiography presented non-critical one-vessel disease or had not critical disease of the left main coronary artery. However, we observed that severe coronary heart disease may be also pre-

sent when normal SPECT is associated with positive exercise ECG, suggesting this should be considered an indication for coronary angiography, especially when the risk factor such as a diabetes or smoking are found.

Conclusions

In conclusion, our study indicates that the long-term survival among a patient cohort with a normal exercise SPECT study is influenced by the number of concomitant CAD risk factors. Our results, substantially underscore the importance of modifying CAD risk factors among patients with a normal SPECT. However, we observed that severe coronary heart disease may be present when normal SPECT is associated with positive exercise ECG, suggesting this should be considered an indication for coronary angiography. Notably, while our study only assessed patients with normal SPECT study, future study should also examine how the assessment of CAD risk factors modifies the risk associated with any level of exercise-induced myocardial perfusion defect.

References

1. Barrett-Connor E, Khaw K. Family history of heart attack as an independent predictor of death due to cardiovascular disease. *Circulation* 1984; 69: 1065–1069.
2. Wackers FJTh, Russo DJ, Russo D, Clements JP. Prognostic significance of normal quantitative planar thallium-201 stress scintigraphy in patients with chest pain. *J Am Coll Cardiol* 1985; 6: 27–30.
3. Doyle JT, Dawber TR, Kannel WB, Kinch SH, Kahn HA. The relationship of cigarette smoking to coronary heart disease; the second report of the combined experience of the Albany, NY and Framingham, Mass. studies. *JAMA* 1964; 190: 886–890.
4. Pamela FX, Gibson RS, Watson DD, Craddock GB, Sirowatka J, Bel-ler GA. Prognosis with chest pain and normal thallium-201 exercise scintigrams. *Am J Cardiol* 1985; 55: 920–926.
5. Haffner SM, Lehto S, Ronnema T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med* 1998; 339: 229–234.
6. Wahl JM, Hakki AH, Iskandrian AS. Prognostic implications of normal exercise thallium-201 images. *Arch Intern Med* 1985; 145: 253–256.

7. Lloyd-Jones DM, Wilson PW, Larson MG et al. Lifetime risk of coronary heart disease by cholesterol levels at selected ages. *Arch Intern Med* 2003; 163: 1966–1972.
8. Staniloff HM, Forrester JS, Berman DS, Swan HJC. Prediction of death, myocardial infarction, and worsening chest pain using thallium scintigraphy and exercise electrocardiography. *J Nucl Med* 1986; 27: 1842–1848.
9. Neaton JD, Blackburn H, Jacobs D et al. Serum cholesterol level and mortality findings for men screened in the Multiple Risk Factor Intervention Trial. Multiple Risk Factor Intervention Trial Research Group. *Arch Intern Med* 1992; 152: 1490–1500.
10. Koss JH, Kobren SM, Grunwald AM, Bodenheimer MM. Role of exercise thallium-201 myocardial perfusion scintigraphy in predicting prognosis in suspected coronary artery disease. *Am J Cardiol* 1987; 59: 531–534.
11. Neaton JD, Wentworth D. Serum cholesterol, blood pressure, cigarette smoking, and death from coronary heart disease. Overall findings and differences by age for 316,099 white men. Multiple Risk Factor Intervention Trial Research Group. *Arch Intern Med* 1992; 152: 56–64.
12. Heo J, Thompson WO, Iskandrian AS. Prognostic implications of normal exercise thallium images. *Am J Noninvas Cardiol* 1987; 1: 209–212.
13. Stamler J, Neaton JD, Wentworth DN. Blood pressure (systolic and diastolic) and risk of fatal coronary heart disease. *Hypertension* 1989; 13: 12–112.
14. Brown KA, Rowen M. Prognostic value of a normal exercise myocardial perfusion imaging study in patients with angiographically significant coronary artery disease. *Am J Cardiol* 1987; 59: 531–534.
15. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation* 1998; 97: 1837–1847.
16. Raiker K, Sinusas AJ, Wackers JT, Zaret BL. One-year prognosis of patients with normal planar or single photon emission computed tomographic technetium 99m-labeled sestamibi exercise imaging. *J Nucl Cardiol* 1994; 1: 449–456.
17. Lloyd-Jones DM, Leip EP, Larson MG, D'Agostino RB, Beiser A, Wilson PW, et al. Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. *Circulation* 2006; 113: 791–798.
18. Elhendy A, Schinkel A, Bax JJ, van Domburg RT, Poldermans D. Long-term prognosis after a normal exercise stress Tc-99m sestamibi SPECT study. *J Nucl Cardiol* 2003; 10: 261–266.
19. McCully RB, Roger VL, Mahoney DW et al. Outcome after normal exercise echocardiography and predictors of subsequent cardiac events: Follow-up of 1,325 patients. *J Am Coll Cardiol* 1998; 31: 144–149.
20. Pavin D, Delonca J, Siegenthaler M, Doat M, Rutishauser W, Righetti A. Long-term (10 years) prognostic value of a normal thallium-201 myocardial exercise scintigraphy in patients with coronary artery disease documented by angiography. *Eur Heart J* 1997; 18: 69–77.
21. del Val Gómez M, Gallardo FG, Salazar ML, Terol I. Valor pronóstico de los estudios de perfusión miocárdica con Tl-201 normal en pacientes con ergometría positiva. *Rev Esp Cardiol* 2002; 55: 991–994.
22. Shaw LJ, Berman DS, Maron DJ et al. Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: Results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial nuclear substudy. *Circulation* 2008; 117: 1283–1291.
23. Berman DS, Hachamovitch R, Kiat H et al. Incremental value of prognostic testing in patients with known or suspected ischemic heart disease: A basis for optimal utilization of exercise technetium-99 m sestamibi myocardial perfusion single-photon emission computed tomography. *J Am Coll Cardiol* 1995; 26: 639–647.
24. Hachamovitch R, Hayes S, Friedman JD et al. Determinants of risk and its temporal variation in patients with normal stress myocardial perfusion scans. What is the warranty period of a normal scan? *J Am Coll Cardiol* 2003; 41: 1329–1340.
25. Hachamovitch R, Berman DS, Kiat H et al. Effective risk stratification using exercise myocardial perfusion SPECT in women: Gender-related differences in prognostic nuclear testing. *J Am Coll Cardiol* 1996; 28: 34–44.
26. Gibbons RJ, Hodge DO, Berman DS et al. Long-term outcome of patients with intermediate-risk exercise electrocardiograms who do not have myocardial perfusion defects on radionuclide imaging. *Circulation* 1999; 100: 2140–2145.
27. Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Berman DS. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. *Circulation* 2003; 107: 2900–2907.
28. Hachamovitch R, Berman DS, Kiat H et al. Exercise myocardial perfusion SPECT in patients without known coronary artery disease: Incremental prognostic value and use in risk stratification. *Circulation* 1996; 93: 905–914.
29. Hachamovitch R, Berman DS, Kiat H, Cohen I, Friedman JD, Shaw LJ. Value of stress myocardial perfusion single photon emission computed tomography in patients with normal resting electrocardiograms: An evaluation of incremental prognostic value and cost-effectiveness. *Circulation* 2002; 105: 823–829.
30. Chaowalit N, McCully RB, Callahan MJ, Mookadam F, Bailey KR, Pellikka PA. Outcomes after normal dobutamine stress echocardiography and predictors of adverse events: Long-term follow-up of 3014 patients. *Eur Heart J* 2006; 27: 3039–3044.
31. Sozzi FB, Elhendy A, Roelandt JR et al. Long-term prognosis after normal dobutamine stress echocardiography. *Am J Cardiol* 2003; 92: 1267–1270.
32. Ladenheim ML, Pollock BH, Rozanski A et al. Extent and severity of myocardial hypoperfusion as predictors of prognosis in patients with suspected coronary artery disease. *J Am Coll Cardiol* 1986; 7: 464–471.